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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,461	02/12/2004	Erika Hawkins	341.022US1	2264
21186 7590 03/13/2009 SCHWEGMAN, LUNDBERG & WOESSNER, P.A. P.O. BOX 2938 MINNEAPOLIS, MN 55402				
EXAMINER HANLEY, SUSAN MARIE				
ART UNIT		PAPER NUMBER		
1651				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/777,461

**Applicant(s)**

HAWKINS ET AL.

**Examiner**

SUSAN HANLEY

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-12, 14-56, 63-67 and 69-73 is/are pending in the application.
- 4a) Of the above claim(s) 2, 4, 5, 9-11, 16-21, 25-32, 37, 45, 46, 48, 53, 63 and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 6-8, 12, 14, 15, 22-24, 33-36, 38-44, 47, 49-52, 54-56, 65-67 and 69-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 10/11/08.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

The amendment and reply filed 11/10/08 are acknowledged.

Claims 1-12, 14-56, 63-67 and 69-73 are pending.

### ***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1-42, 56 and 69; and the following specie election:

A. Quenching agent for the first or second enzyme-mediated reaction: a sequestering agent that is a nonionic detergent;

B. First enzyme-mediated luminescence reaction: *Renilla reniformis* luciferase-mediated;

C. Second enzyme-mediated luminescence reaction: *Photinus pyralis* luciferase-mediated;

in the reply filed on 1/31/07 is again acknowledged. Applicants' traversal was found persuasive, in part. Groups I and II (method and kit) were rejoined insofar as they read on the elected species.

Claims 2, 4, 5, 9-11, 16-21, 25-32, 37, 45, 46, 48, 53, 63 and 64 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/07.

Claims 1, 3, 6-8, 12, 14, 15, 22-24, 33-36, 38-44, 47, 49-52, 54-56, 65-67 and 69-73 remain under examination. Claims drawn to an anthozoan luciferase or a peroxidase will be examined insofar as they read on an anthozoan luciferase.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

*Response to Arguments*

*Claim Rejections - 35 USC § 112*

Claims 1, 3, 6-8, 12, 14, 15, 22-24, 33-36, 38-44, 47, 49-52, 54-56, 65-67 and 69-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining luminescence energy produced by a first and second luciferase-mediated luminescence reaction wherein at least one of said luciferases is anthozoan and the luminescence generated by the anthozoan luciferase is selectively quenched by protected coelenterazines; colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19 of the specification; and nonionic detergents that are not polyethylene glycol octylphenylether or polyoxyethylene sorbitan monolaurate prior to initiating the second luminescent reaction; and determining the luminescence produced by the second reaction; and a kit thereof, does not reasonably provide enablement for said method or kit wherein the first enzyme mediated reaction is provided by any possible substrate analog inhibitor for an anthozoan luciferase or a protected coelenterazine or any possible colored compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicants request clarification on the status of claims 70-73, submitted with the Amendment filed on April 9, 2008, since they were not rejected. Applicant asserts that claims 44, 55 and 56 are enabled. That is because claims 44, 55 and 56 recite anthozoan luciferase, and a nonionic detergent that is not polyethylene glycol octylphenylether or polyoxyethylene sorbitan monolaurate or a yellow colored compound.

Applicant argues that the disclosure that substrate analog inhibitors of luminescence reactions, e.g., protected coelenterazines that are substrate analog inhibitors of an anthozoan luciferase, nonionic detergents and certain colored compounds, for instance, those that quench red, blue or green light, can inhibit luminescence mediated by enzymes such as an anthozoan luciferase without substantially inhibiting a subsequent luminescence reaction, i.e., those agents are selective quench reagents, it is within the skill of the art to identify specific protected coelenterazines that are substrate analog inhibitors, specific nonionic detergents and specific colored compounds that quench red, blue or green light, other than those in the working examples in the specification, that are selective quench reagents for an anthozoan luciferase-mediated luminescence reaction.

Applicant submits that although Sherf discloses agents that selectively quench a firefly luciferase-mediated reaction, Sherf et al. evidence that identifying selective quench reagents for enzyme-mediated luminescence reactions is within the skill of the art.

Applicant argues that detailed knowledge of the active site of an enzyme is not needed to practice Applicant's invention. Methods to determine whether an agent is an inhibitor or a substrate for an enzyme were well known to the art prior to Applicant's invention as per the documents: Denberg et al., Filippova et al., Farace et al., and White et al. Applicant further argues that the Examiner cannot reasonably be contended that a program to locate biomolecules with target biological or physical properties would not be carried out by the art because the results cannot be predicted in advance. Applicant cites . In re Wands, 8 U.S.P.Q.2d 1400, 1406-1407 (Fed. Cir. 1988), to support the argument that methodologies required to carry out extensive synthesis and screening programs to locate biomolecules with particular properties do not constitute undue experimentation. In re Wands, was directed to the screening of negative hybridomas in order to find one that makes the desired antibody.

Applicant asserts that practitioners in the art related to the present application would be well-equipped to screen various agents to identify those that selectively quench an anthozoan luciferase-mediated reaction but not another enzyme-mediated luminescence reaction. See also, Hybritech Inc. v. Monoclonal Antibodies Inc., 231 U.S.P.Q. 81, 84 (Fed. Cir. 1986) (evidence that screening methods used to identify characteristics [of monoclonal antibodies] were available to art convincing of enablement). Thus, the fact that a given claim may encompass a variety of quenching agents is not dispositive of the enablement issue, particularly in an art area in which the level of skill is very high and in which screening of large numbers of compounds has

been standard practice for at least ten years (Ex parte Forman, 230 U.S.P.Q.2d 456 (Bd. App. 1986)).

Applicant's arguments that it is within the skill of the art to identify specific protected coelenterazines that are substrate analog inhibitors is persuasive and the rejection or modified accordingly. However, Applicant's argument regarding Sherf and the named references show that methods to determine whether an agent is an inhibitor or a substrate for an enzyme were well known to the art prior to Applicant's invention as per the documents has been considered but is non-persuasive. All of the cited references are directed to the bioluminescent reaction catalyst by firefly luciferase which is a different enzyme than anthozoan luciferase. Likewise, Applicant arguments regarding the cited case law is not relevant to the rejection because the cases are directed to a different art, that of screening for monoclonal antibodies.

The design of enzyme inhibitors requires detailed knowledge about the active site of an enzyme. Without some disclosure regarding the active site, the skilled artisan could not predict which compounds based on the disclosed generic structure would be inhibitors and not substrates for the anthozoan luciferase. Hence, the skilled artisan would have to resort to trial and error testing of compounds to find inhibitors and not substrates. Such a trial and error process clearly amounts to undue experimentation. this does not constitute a search for a prediction of what would successfully inhibit anthozoan luciferase but rather, with the exception of the colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19 of the specification; and nonionic detergents that are not polyethylene glycol octylphenylether or polyoxyethylene sorbitan monolaurate, what compounds of other structures (e.g., structures related to those same *supra*) would the skilled artisan have a reasonable

expectation that they would inhibit the anthozoan luciferase. Such an endeavor is a *de novo* undertaking and the specification does not address this problem.

Claims 44, 55 and 56 are not enabled, at least in part, because they are drawn in the alternative to protected coelenterazine and a nonionic detergent that is not PEG or octylphenylether or polyoxyethylene sorbitan monolaurate or to an inhibitor that is any yellow (claims 44 and 55), red, blue or green (claim 65) light that quenches the reaction. The claim are enabled only for colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19 of the specification. Otherwise, the skilled artisan would have to find a starting point *de novo* to determine structures of compounds other than those indicated that might inhibit the luciferase. The skilled artisan can screen compounds *ad nauseum*. However, the instant disclosure does not provide guidance beyond compounds of other structures, or the design thereof, that would have a reasonable expectation of inhibiting the anthozoan luciferase.

Regarding claims 70-73, it is obvious that they were meant to be rejected by this scope rejection as they are drawn in the alternative to any compound that emits blue, green or red light for the reasons explained above.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after



the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susan Hanley/  
Examiner, Art Unit 1651

/Irene Marx/  
Primary Examiner  
Art Unit 1651

